CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214120Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

IND 074618

MEETING MINUTES

Celgene Corporation
Attention: Mary Vandekauter, M.S., RAC
Director, Regulatory Affairs
9225 Indian Creek Parkway, Suite 900
Overland Park, KS 66210

Dear Ms. Vandekauter:

Please refer to your investigational new drug application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for azacytidine.

We also refer to the meeting between representatives of your firm and the FDA on November 21, 2019. The purpose of the meeting was to discuss a proposed marketing application for oral azacitidine.

A copy of the official minutes of the meeting/telecon is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Rachel McMullen, Senior Regulatory Project Manager at (240) 402-4574.

Sincerely,

{See appended electronic signature page}

Donna Przepiorka, MD, PhD
Clinical Team Lead
Division of Hematologic Malignancies 1
Office of Oncologic Diseases
Center for Drug Evaluation and Research

Enclosure:

- Meeting Minutes

U.S. FOOD & DRUG ADMINISTRATION

MEMORANDUM OF MEETING MINUTES

Meeting Type: B
Meeting Category: Pre-NDA

Meeting Date and Time: November 21, 2019; 10:00 AM to 11:00 AM (ET)
Meeting Location: 10903 New Hampshire Avenue
White Oak Building 22, Conference Room: 1419
Silver Spring, Maryland 20903

Application Number: IND 074618
Product Name: Azacitidine
Indication: (b) (4)

Sponsor Name: Celgene Corporation

Meeting Chair: Donna Przepiorka, MD, PhD
Meeting Recorder: Suria Yesmin, MS

FDA ATTENDEES

Division of Hematological Malignancies (DHM1)
R. Angelo de Claro, MD, Director (Acting)
Donna Przepiorka, MD, PhD, Clinical Team Leader
Emily Jen, MD, PhD Clinical Reviewer
Patricia Dinndorf, MD, Clinical Reviewer
Suria Yesmin, MS, Senior Regulatory Project Manager

Office of Biostatistics, Division of Biometrics V
Yute Wu, PhD, Acting Biometrics Team Leader
Qing Xu, PhD, Biometrics Reviewer

Office of Clinical Pharmacology
Olanrewaju Okusanya, Pharm D, Clinical Pharmacology Team Lead
Vicky Hsu, Pharm D, Clinical Pharmacology Reviewer

Office of Pharmaceutical Quality
Anamitro Banerjee, PhD, Branch Chief

SPONSOR ATTENDEES

Celgene Corporation
Jay Backstrom, MD, Chief Medical Officer
Paul McInulty, BS Vice President, Regulatory Affairs
Mary Vandekauter, MS, Director, Regulatory Affairs

Carrie Brownstein, MD, Vice President, Clinical R&D
Charles Beach, PharmD, Executive Medical Director, Clinical R&D
Ignazia La Torre, MD, Sr. Medical Director, Clinical R&D
Keshava Kumar, PhD, Principal Clinical Research Scientist, Clinical R&D
Qian Dong, PhD, Associate Director, Biostatistics
Nanxiang Ge, PhD, Executive Director, Biostatisticas
Allison Gaudy, PhD, Sr. Scientist, Pharmacokinetics
Rochelle, Bailey, MD, Sr Director, Lead Global Safety Physician
Christine Stuhlmiller, MBA, Sr Director, Global Project Leader
Daniel Lopes de Menezes, PhD, Associate Director, Translational Development

1.0 BACKGROUND

CC-486, an oral formulation of azacitidine, is being developed by Celgene Corporation, the Sponsor, for treatment of AML (b) (4) The Sponsor is planning to submit an NDA for CC-486 in 1Q 2020 (b) (4) Advice on the content and format of the NDA was provided in Type C Written Responses issued on October 24, 2019.

On September 27, 2019, the Sponsor requested a Type B meeting to obtain FDA's feedback on the adequacy of the results of Study CC-486-AML-001 to support submission of an NDA.

FDA sent Preliminary Comments to Celgene on November 14, 2019.

2.0 DISCUSSION

Question 1: *Does the Agency agree that the efficacy results for the primary endpoint of OS in conjunction with the results of the key secondary endpoint of RFS demonstrate a statistically significant and meaningful clinical benefit of CC-486 in this patient population?*

FDA Response to Question 1: Your analysis demonstrates statistical significance according to the prespecified plan. Whether the efficacy results are clinically meaningful will be a review issue. We remind you that the data from CC-486-AML-001 should be supported by data from treatment trials of AML (see response to Question 4, Type C WRO dated10/24/19).

DISCUSSION: The Agency agreed that the Sponsor's plan to include three Phase 1 studies along with AZA-AML-001 in the SCE is acceptable. The Agency clarified that the ISE dataset should therefore include all 5 trials. The Agency also reminded the Sponsor that the maximum page limit of the Clinical Summary text (Modules 2.7.1 through 2.7.4) in total is 400 pages.

Question 2: *Does the Agency agree that the safety profile of CC-486 observed in the pivotal Phase 3 study, Study CC-486-AML-001 is supportive of an NDA for CC-486* (b) (4)

[redacted]

a) *Does the Agency agree that the safety profile of CC-486 observed in the pivotal Phase 3 study, Study CC-486-AML-001 and consistent with the established safety profile for azacitidine is acceptable to enable filing of the proposed NDA?*

FDA Response to Question 2a: The safety data from CC-486-AML-001 alone are not sufficient for submission of an NDA; the submission should include safety data from other trials in your development program. See responses to Questions 5-8 in the Type C WRO dated 10/24/19. Whether the totality of the safety data is sufficient for filing the proposed NDA will be a review issue.

DISCUSSION: There was no discussion.

b) *Despite relapse free survival being defined as the key secondary endpoint, per protocol, AML relapse and disease progression were reported as adverse events. Does the Agency agree with the Celgene proposal to present primary safety data for this study excluding AML relapse-associated events to allow for a more informative and clear interpretation of the safety profile of CC-486?*

FDA Response to Question 2b: We have no objection to your plan to exclude AML relapse/disease progression preferred terms as adverse events for the review of safety. In your submission, please provide a list of the preferred terms excluded from the analysis.

DISCUSSION: There was no discussion.

c) *Does the Agency have any comments on the overall safety data package presented in this pre-NDA meeting package to support the review of the upcoming NDA?*

FDA Response to Question 2c: See response to 2a.

DISCUSSION: There was no discussion.

Question 3: *Does the Agency agree that the efficacy and safety data from Study CC-486-AML-001, a Phase 3, Double-blind, Randomized, Placebo-Controlled Study to Compare the Efficacy and Safety of Oral Azacitidine (CC-486) Versus Placebo as Maintenance Therapy in Subjects with Acute Myeloid Leukemia are adequate for filing and review of the NDA for the proposed indication?*

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